

INTRODUCTION.

The treatment of varicose veins has assumed in recent years a prominent aspect, due chiefly to the discovery that it was possible to cure a large number of cases by means of intra-venous injections. provided that

BY INTRA-VENOUS INJECTIONS. provided that the same could be carried out

By

J.D.P. McLatchie, M.B., C.M. (Ed.)

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in this portion of the

M.D., 1928.



(4) Remarks on the different substances used  
for intra-venous injections.

INTRODUCTION.

(5) Technique

(6) Results of treatment.

The treatment of varicose veins has assumed in recent years an entirely different aspect, due chiefly to the work of Sicard. He showed that it was possible to cure them in the great majority of cases by means of intra-venous injections and that this cure, provided that certain conditions were observed could be carried out without danger to the patient.

I have endeavoured in this Thesis to record the results in my own hospital and private practice of the above mentioned treatment as well as the experience of some of the numerous workers in this portion of the therapeutic field.

With this object in view I have considered the subject under the following heads:

- (1) Historical
- (2) Preparation and dosage of the various chemical substances used in the modern treatment of varices.
- (3). Local and general effects of the injections.

- (4) Remarks on the different substances used for intra-venous injection.
- (5) Technique.
- (6) Results of treatment.
- (7) Contra-indications.
- (8) Advantages of the method.
- (9) Summary.
- (10) Bibliography.

always the result.

Calver<sup>1</sup> either cut the veins out, or cauterized them by a cautery of red heat after exposing the veins by incision. He said that there must be the use of care the edges of the skin incision.

Ambroise Paré<sup>2</sup> also recommended the cautery.

Paulus Argente<sup>3</sup> exposed the vein by an incision and passed a needle with a double thread through it. He next opened the vein and allowed the blood to escape as far as possible. He then tied the vein at the upper part of the wound and more blood was regulated by compressing the limb with the hands. The lower part of the vein was then tied and the part of the vein between the ligatures was either cut or allowed to "drop out" of its own accord.

Ambroise Paré<sup>4</sup> did practically the same operation

## HISTORICAL.

The beginning of the injection treatment of Varicose veins may be said to date from the year 1851 when Pravaz<sup>1</sup> invented his syringe. Before that date the treatment for their radical cure was surgical, thus Hippocrates<sup>2</sup> advised multiple puncture of the vein and said that they should not be cut open as then large ulcers may result.

Celsus<sup>3</sup> either cut the veins out, or destroyed them by a cautery at red heat after exposing the veins by incision. He said that care must be taken not to burn the edges of the skin incision. Avicenna<sup>4</sup> also recommended the cautery.

Paulus Aegineta<sup>5</sup> exposed the vein by an incision and passed a needle with a double thread beneath it. He next opened the vein and allowed as much blood to escape as was desired. He then tied the vein in the upper part of the wound and more blood was evacuated by compressing the limb with the hands. The lower part of the vein was then tied and the part of the vein between the ligatures was either cut or allowed to "drop out" of its own accord.

Ambroise Paré<sup>6</sup> did practically the same operation



as P. Aegineta, only he destroyed the vein between the ligatures with a cautery.

Pravaz used his syringe to inject aneurisms with perchloride of iron and to cure them by coagulating the blood in them.

This idea was soon applied to the treatment of varicose veins and the substances used were such as were considered likely to produce a clot sufficient to obliterate the lumen of the vein.

The great cause of failure in the earlier applications of this treatment was of course the ignorance of antisepsis, at that period, and as a result septic complications, such as local abscesses, sloughs and septic emboli prevented the general adoption of the treatment in spite of the success obtained in many instances.

Members of the Lyons school were the first to use the new method of treatment. Desgranges, Valette<sup>7</sup>, Barrier and Petriquin<sup>8</sup> injected perchloride of iron into the veins and had some successful results.

The treatment initiated by the Lyons school was taken up in 1853 by Chassaignac<sup>9</sup> of the Saint-Antoine Hospital of Paris. He used the same drug but soon

says, so that his treatment could not be called successful.

gave up the treatment on account of the number of cases in which sepsis ensued.

The use of Perchloride of Iron was given up for a time, especially as in 1854 Desgranges<sup>10</sup> reported the cure of sixteen cases by the injection of 'Liqueur Iodo-tannique' without any symptoms causing anxiety.

The Liqueur Iodo-tannique was a formula due to Socquet and Gullermond of Lyons and its composition as injected into the veins was:

Iodine 5 grammes

Tannin 45 grammes

Water 50 grammes.

the dose usually being 5 - 7 drops.

Desgranges noted that the local reactions were much milder than with perchloride of Iron and he also compared the nature of the clot caused by the two preparations. The Liqueur Iodo-tannique clot was insoluble in boiling water, but soluble in solutions of Hydrochloric acid and in solutions of Potassium and Sodium Salts, while the clot caused by perchloride of Iron was soluble in boiling water and only slightly soluble in alkaline media.

Desgranges kept his patients in bed for twelve days, so that his treatment could not be called ambulatory, and Delors at the Lyons Congress of Surgery in 1894 expressed his belief in it and also maintained that

ory. Septic infection, however, was still experienced in a more extended use of this substance.

The next step was to try perivenous injections with the object of setting up an inflammation which would spread to the inner coat of the vein and so cause thrombosis. It was also thought that the risks of septic emboli might be lessened.

The first substance tried was ergot of rye. It was employed by Guyon and others in 1876 with unhappy results and was therefore soon abandoned.

In 1878 Englisch of Vienna<sup>11</sup> used 5% alcohol; Marc Sée and Broca adopted Englisch's method and Broca also modified it by using 30% alcohol.

Broca<sup>12</sup> also tried Perchloride of Iron and Papi employed chloral Hydrate. The results of the perivenous injections were no better than the old, some successes but many failures chiefly due to septic infection.

In 1881 Legendre<sup>13</sup> revived the Liqueur Iodo-tannique method. He modified it by using a much weaker solution (1000 grammes of water instead of the 50 of the original formula) but his results were no better than those obtained by the stronger solution. This method was, however, still used in France by a few medical men, and Delore at the Lyons Congress of Surgery in 1894 expressed his belief in it and also maintained that



its efficacy was due not to coagulating the blood but to the inflammation set up in the walls of the vein.

In 1904 Tavel<sup>14</sup> of Berne introduced Carbolic Acid. He used a 5% solution and injected it after ligaturing the internal saphenous vein.

In 1908 Schiassi<sup>15</sup> injected into the vein a solution composed of:

Iodine	gramme 1
Pot. Iodid	gramme 1.60
Water	grammes 100.

He divided the vein below the knee and through a cannula tied into the distal end of the divided vein, he injected 30-50 c.c. of the above solution. He then ligatured the vein below the point of the cannula.

In 1916 Linser of Tubigen<sup>16</sup> used Perchloride of Mercury. He treated many cases with it, and there is no doubt that this method was a great advance. It however caused nephritis, stomatitis, enteritis, in a certain number of cases.

The medical profession, nevertheless, as a whole, looked askance at the method of treating varicose veins by intravenous injections, and it was not until the work of Sicard especially and of Genevrier that the method has



and a later paper in 1922<sup>21</sup> Montpellier and Lacroix become established on a firm basis and has obtained published their results with Bimiodide of Mercury in general recognition.

1921<sup>22</sup> and in 1924 J. Troisier<sup>23,24</sup> introduced Citrate of Soda. The above and various other substances will be noticed that the veins into which he injected that drug, became obliterated and that no emboli were produced. He considered this result to be due to the Soda part of the Salt, and in 1917 he began his intravenous injection treatment of varices by injecting Carbonate of Soda. In 1919 he showed before a medical society<sup>17</sup> his first series of cases, and in 1920 he published his first paper<sup>18</sup> on the subject. With increasing experience, however, he found that this substance was too caustic and as a result its injection required so much care that it was not suitable for general use. After trying various salts, such as Chloride of Calcium, Hyposulphite of Soda, etc. he finally chose Salicylate of Soda<sup>19</sup> and this is still the drug that he recommends for treatment.

Génévrier also figures prominently in the development of this treatment. In 1917 he noticed the obliteration of veins following the intravenous introduction of Quinine. He published his method of treatment in 1921<sup>20</sup>

and a later paper in 1922.<sup>21</sup> Montpellier and Lacroix published their results with Biniodide of Mercury in 1921<sup>22</sup> and in 1924 J. Troisier<sup>23,24</sup> introduced Citrate of Soda. The above and various other substances will be considered in the following section.

Pure On the preparation and dosage of the various chemical substances employed in the modern treatment of Varices.

The substances are of course used in solution; the water employed should be twice distilled and carefully sterilised. An appropriate amount is put up in glass ampoules and these are again sterilised.

The ampoules are usually made of neutral glass. The solutions usually keep well in this. The only drug that causes any difficulty is Sod Salicylate. It should not be put up in amber coloured glass as with that, owing to the Iron in the glass, a precipitate is formed of Salicylate of Iron. Even when the glass is clear and neutral some change takes place. This is indicated by a slight brownish discolouration of the solution. The nature of this change is not understood. It can be prevented by adding Sod. Thiosulphate to the solution in the proportion of 1.5000. The solution of Sod-Salicylate then remains perfectly clear. This modified solution is the one I always use.

at the first sitting only 2 c.c. of the 20% solution should be injected.

Pure crystallised Carbonate of Soda.

This is not generally used now on account of its powerful caustic action. If injected by mischance into the perivenous tissues, or if blood mixed with it leaks from the vein, extensive sloughing may result.

It is usually put up in 10 c.c. ampoules containing a 10% solution. For the first injection a 5% solution should be used. If necessary a 15% solution may be employed.

Genevri's formula is:

Before injecting the Sod. Carb. solution, a needle fitted to a 2 c.c. syringe containing normal saline ought to be passed into the vein. The normal saline is then injected and if it remain entirely in the vein, the syringe is detached and a 10 c.c. syringe containing the Sod. Carb. solution is attached to the needle and the solution injected.

Sodium Salicylate.

This is the drug which is most generally used at present. It is put up in 3 strengths, 20% - 30% and 40%. Each ampoule contains 2 c.c. or 3 c.c. Of course larger sizes may be used if the operator wishes to do so. At the first sitting only 2 c.c. of the 20% solution should be injected.



At subsequent sittings the maximum amounts to be injected are:

8 - 10 c.c. of the 20% solution.

8 c.c. " " 30% "

5 - 6 c.c. " " 40% "

These amounts are not absolute, but form a good working guide.

The double Hydrochloride of Quinine and urea is used

### Quinine.

Genévrier's formula is:

Quinine Hydrochloride (neutral) 4 grammes

Urethane 2 grammes

Aq. Distill. 30 c.c.

The urethane being used for its anaesthetic properties.

The quinine crystallises out so that the ampoules have to be warmed immediately before use.

This difficulty can be overcome by using the Bihydrochloride of Quinine. This remains in solution and avoids the necessity of previous warming of the ampoules.

For the first injection not more than a total amount of 2 c.c. should be used. This is introduced

by multiple punctures at intervals of 2-4 inches, each site receiving  $\frac{1}{4}$  -  $\frac{1}{2}$  c.c.

At subsequent sittings amounts up to 6 c.c. can be used each time.

If the vein is large, as much as 1 c.c. can be introduced at one place if necessary.

The double Hydrochloride of Quinine and urea is used by Vandier<sup>25</sup>. He employs it in strengths of 5%, 10%, 12%, 15% and 20%. He started using it on the suggestion of Le Blaye. The combination had of course been long used in surgery on account of its local anaesthetic effects and it was thought that this would lessen the painful effects of intravenous injections. He states that it does so but apart from this there is not much evidence of any advantage over Genevrier's formula, and in the weaker dilutions its action seems uncertain, but he says he has never failed to get a reaction with the 20% solution.

In a later publication<sup>26</sup> Vandier has given up the use of the weaker solutions and uses solutions varying in strength from 15-30%.

In the few instances in which I have used this preparation there was an entire absence of any cramp like

pains.

Biniodide of Mercury (Montpellier).

1. Usual formula is

Biniodide of Mercury	1
Sodium Iodide	1
Aq. distill.	100

2. Another formula is:

Biniodide of Mercury.	50 grammes
Sod. Iodid	.50 grammes.
Sod. Chlor.	.50 "
Aq. distill.	100 c.c.

For the first dose 1-2 c.c. are injected. As much as 6 c.c. of solution No. 1 (the one usually employed) has been injected at one sitting, but this caused salivation and diarrhoea. Solution No. 2 being weaker can be given in larger doses.

Sodium Citrate (Troisier).

The formula for this is:

Sod. Citrate (pure)	) a a 8 grammes.
Aq. Distill.	

Formerly this was the quantity injected at each sit-

ting, except the first, when about 4 c.c. were injected. Through each puncture 1-2 c.c. were introduced, the punctures being about 3-5 centimetres apart. At the present time, the usual strength to begin with is only about 5% and the strength is increased according to the results. It is rarely necessary to use the 100% solution. When the patient notices a salty taste in his mouth, no more should be given.

Sodium Chloride. This was introduced by Linser<sup>27,28</sup> after he gave up the use of Hyd. Perchlor. He used a 15-20% solution. The quantity injected at one sitting is usually 5-10 c.c. Larger quantities can be used if necessary as it is not toxic. For patients of an advanced age it may be necessary to use a stronger solution.

Meisen's Solution. Meisen first used Sod. Sal. in 20%-30% solution in 1925<sup>29</sup>. but in 1927<sup>30</sup> he modified his formula to a solution composed of

Sol. Sod. Salicylate	25%	} $\overline{a} \overline{a}$
Sol. Sod. Chlorid.	10%	

He found by experience that the maximum dose for one sitting ought not to exceed 10 c.c.



Glucose. F. Remmovsky and R. Kantor<sup>31</sup> introduced glucose. They used a 50% solution, in amounts of 5-10 c.c. for one sitting. Glucose can also be used in strengths up to 66%.

The effects alluded to in this section are those of a preparation called Calorose has been introduced which follows a strictly intravenous injection. Should by G. Nobl<sup>32</sup>. It consists of equal quantities of Dextrose and Levulose in distilled water. The strength of the solution is 50%. As these sugars are not poisonous, larger quantities than 10 c.c. can be given. long time to heal and may result in disfiguring scars.

As a rule the strictly intravenous injection is painless apart from the slight pain caused by the needle puncture. Some patients say it is uncomfortable and a few say they have pain. The latter are usually nervous people who are having their first injection.

Very soon after the injection (e.g. a few seconds) a contraction of the vein may sometimes be seen. It is very curious to note how even a large vein may contract up for several inches of its course and become hardly noticeable for some time afterwards. Erection of the hairs of the skin in the neighbourhood of the injection may be noticed and occasionally the surrounding skin becomes pale. The symptom most distressing to the patient

is, however, Remarks on the local and general effects of the injections. comes on a few seconds after the injection, and indeed it may come on while a solution of 40% is being given. The patients

The effects alluded to in this section are those usually say it shoots down the leg into the foot, but which follow a strictly intravenous injection. Should some have described it as also passing up the thigh, the solution be injected into the tissues outside the vein, severe inflammation is apt to follow, and even sloughing may result. The resulting ulcers take a long time to heal and may result in disfiguring scars. It is relieved by elevating and supporting the leg, or by

As a rule the strictly intravenous injection is allowing the patient to lie down, painless apart from the slight pain caused by the needle puncture. Another local effect is great swelling of the vein in the neighbourhood of the injection. This is even a few say they have pain. The latter are usually nervous people who are having their first injection.

Very soon after the injection (e.g. a few seconds) rather alarming when observed for the first time, but no a contraction of the vein may sometimes be seen. It is anxiety need be felt as the swelling passes away in a few very curious to note how even a large vein may contract

up for several inches of its course and become hardly noticeable for some time afterwards. Erection of the hair tissues near the site of puncture. This is of course hairs of the skin in the neighbourhood of the injection due to the leaking of blood from the puncture in the vein may be noticed and occasionally the surrounding skin becomes pale. Strictly speaking it ought not to occur, but it is not always possible to avoid it even with the greatest

is, however, "cramp", and this occurs chiefly with the Sod. Salicylate injections. The cramp comes on a few seconds after the injection, and indeed it may come on while a solution of 40% is being given. The patients usually say it shoots down the leg into the foot, but some have described it as also passing up the thigh. It is most probably a reflex due to irritation of the nerves in the venous wall. It is always bearable and only lasts a minute or so at the most in my experience. It is relieved by elevating and supporting the leg, or by allowing the patient to lie down.

Another local effect is great swelling of the vein in the neighbourhood of the injection. This is seen especially when quinine is injected into a vein which runs over bony surfaces, e.g. foot and front of tibia. It is rather alarming when observed for the first time, but no anxiety need be felt as the swelling passes away in a few days at most.

Extravasation of blood may occur into the extravascular tissues near the site of puncture. This is of course due to the leaking of blood from the puncture in the venous wall. Strictly speaking it ought not to occur, but it is not always possible to avoid it even with the greatest

care. It causes temporary disfigurement merely, unless some of the injected substance is mixed with it. In that case a swelling will remain for a considerable time, and even necrosis may result.

On the day following the injection, if the result is successful the vein for a variable distance feels tender and hard. The degree of tenderness varies of course with the amount of inflammatory reaction of the venous wall. This is sometimes quite severe, and then the skin over the affected part is red and feels hot. At other times when the reaction is slight, hardly anything is noticed locally except a hardening of the vein. The patient often says that the leg is rather stiff for the next two or three days, especially on getting up in the morning. These results are very seldom sufficiently severe to prevent the patients from following their usual occupations, and one patient told me that she even did her "physical jerks" all through the treatment.

The application of a fomentation at night relieves the tenderness in the usual run of moderately severe reactions. In a few cases the reaction may require rest in bed for a day or two. This is especially noticed with Quinine. These acute symptoms usually disappear



in 4-5 days, and in the vast majority of cases need cause no anxiety.

When the inflammation has passed off, there may be pigmentation of the skin over the part. This may take a long time to go and in some cases it never quite disappears. After a variable time, e.g. 2-3 months, the vein is transformed into a fibrous cord.

The general effects except in a small percentage of cases, are quite negligible.

Palpitations, faintness, usually occur during the earlier injections, and are due to fear. Noises in the ears and giddiness may occur after Sod. Sal. and Quinine, and some patients say that they have a bitter taste in the mouth soon after Quinine has been injected.

Skin eruptions have been noticed in a few cases, e.g., urticaria and a patchy erythema.

G. Delater<sup>33</sup> has referred to some of these effects in a recent article. He says that in about  $\frac{1}{2}\%$  of his cases he has noticed slowing of the pulse, cold sweats and nausea. These symptoms occurred at the second or third injection, although nothing had happened at the first injection. He mentions that

the dose given was 4 c.c. 20% Sod. Sal in each leg. On substituting quinine, the reaction did not occur. As regards these cases I think that the patient is rather apprehensive for the first 3 or 4 sittings. The first injection of 2 c.c. 20% Sod. Sal. with only one puncture does not affect them so much as perhaps the next two sittings, when more punctures are made. The symptoms may be due to an idiosyncrasy to Sod. Sal. but it is not unreasonable to consider them as due to emotion to a large extent.

He also mentions a case where 40% Sod. Sal. when injected caused arrest of circulation and respiration for a short time. Another case which had a history of an old phlebitis of the deep veins received 2 injections of 2 c.c. 30% Sod. on different occasions. The first time she felt dazed on the way home; the second time she was found unconscious in the street and had to be taken home in a car. She recovered completely. These seem to be examples of idiosyncrasy to the drug. He mentions also 5 cases in each of which 1 gramme of quinine was injected at one sitting. Soon afterwards they complained of a bitter taste in the mouth and had noises in the ears, palpitation, sweats and nausea. They became

restless, and had waves of heat. The pulse was feeble but regular. There was a slight rise of temperatures, no albumen in the urine. An attack of urticaria supervened. Complete recovery followed. These are evidently also examples of idiosyncrasy to the drug injected.

Aimes of Montpellier<sup>34</sup> states he always uses quinine for his injections. In one case where quinine had failed he twice used 30% Sod. Salicylate at 8 days interval. He gave a third injection this time of 40% Sod. Sal. and the patient was attacked with dyspnea, a sense of oppression and a generalised urticaria which lasted about 2 hours.

Jorgensen<sup>35</sup> had a case (a woman aged 45) in which he gave three injections each of 5 c.c. 20% Sod. Salicylate with satisfactory results as far as the veins were concerned and without any constitutional symptoms. A week after the last injection a further dose of 5 c.c. 20% Sod. Salicylate was given. Two or three hours after this injection the patient had headache, noises in the ears, shivering and free perspiration. Accompanying these symptoms, there was edema of the face and hands. Later urticaria appeared mainly on the face and lower limbs. Petechiae were also found



on the inside of the thighs.

There were also nausea and vomiting, quick and deep breathing and the pulse was quickened.

The temperature was normal, and there was no albumen, blood or sugar in the urine.

After twenty-four hours the whole condition cleared up leaving the patient in an exhausted condition. Previous to the injections this patient had been taking aspirin in rather large doses, but details of the amount taken are not given.

The only case in my own practice in which I have seen unusual symptoms was a woman aged 60 who had extensive varicose veins of both legs and an ulcer on the inner side of the right ankle.

The ulcer was healed by antiseptics and dressings of Unna's Zinc Gelatine and she then agreed to have the veins obliterated. Into a prominent vein leading from the ulcer but well away from it 1.5 c.c. Quinine  $\bar{c}$  Urethane solution was injected. The injection was strictly intravenous and caused no trouble at the time, but when seen a few days later the leg was swollen and edematous and the veins could not be seen. The left leg was therefore treated with the same quantity of the



Quinine and Urethane solution with an exactly similar result.

There were no general symptoms but the patient said her legs were painful and heavy.

The swelling disappeared in a few days with rest and bandaging. A solution of Sod. Salicylate was used instead of Quinine and there were no further troublesome sequelae.

Remarks on the different substances used  
for Intra-venous injection.

Sodium Carbonate: As this is seldom used now owing to its severe effects, it need not be discussed.

Sodium Salicylate: I consider this to be on the whole the best substance to use. The curative inflammatory reaction is generally speaking, mild, and should some of the solution be injected perivenously there is not much risk of necrosis of the tissues. Of course this only applies to small quantities that anyone might inadvertently inject. If any large quantity is so injected, it usually means that the operator is unskilful.

For the first injection never use more than 2 c.c. This is injected by a single puncture.

The tissue reaction is thus tested, and also an idea is obtained of any idiosyncrasy of the patient to the drug.

Should the 20% solution be successful, continue with that strength, of course giving larger quantities if there is no reaction use the 30% solution, and then The great advantage of quinine is the extent of area that

the 40% solution if necessary.

Where the desired effect is not obtained, it is always advisable to work up rapidly to the higher strengths. If the use of a weaker solution is persisted in, the result is merely thickening of the venous wall without obliteration. The treatment can be given two or three times a week. This of course depends on the extent of the varicose veins and the reaction set up. When the 40% solution fails to cure, a different substance ought to be tried. An important point in the injecting of Sod. Salicylate is the occurrence of a characteristic stinging pain when any of the solution escapes into the perivenous tissues. This ought to be a warning to the operator to stop the injection. To wait until he observes a swelling caused by an extravascular injection is a very likely method of producing a slough.

I do not advise adding cocaine (or one of its modifications) to the solution. Its anaesthetic effects may abolish the warning signal of pain when the injection is extravascular.

Quinine. The first injection should not be more than 2 c.c. for the same reasons as given under Sod. Salicylate. The great advantage of Quinine is the extent of area that

can be treated. This is a great saving of time. Unfortunately the local reaction is more severe than with Sod. Salicyl. and if many injections are made it may be necessary for the patient to lie in bed for a few days. This in my experience is a very rare event in those treated by Sod. Salicylate.

Quinine does not give rise to the so-called "cramps" which so frequently follow Sod. Salicylate, and there is not at once so much pain when it is injected extravascularly, but in that case the pain is usually very severe during the next three or four days.

Quinine in my experience is very useful in those cases where Sodium Salicylate has failed. In a case of large and extensive varices, where I could not get a satisfactory result with Sod. Salicylate, a change to Quinine brought about an immediate success.

Quinine should not be used in cases of pregnancy on account of the danger of causing abortion, or during menstruation, as it may cause griping pains.

As a general rule none of the substances used cause clotting of the blood. The result of mixing them with the blood is to cause haemolysis, but with



quinine, especially after two or three punctures, the blood in the syringe may clot. The clots are small but quite obvious to the naked eye. On microscopic examination one finds in addition to the clots, the débris of the <sup>red</sup> corpuscles, from which the haemoglobin has disappeared, collected in masses. With a similar mixture of blood and Sod. Salicylate no clots or masses of débris are to be seen. The only formed cells left in both cases are the leucocytes.

Biniodide of Mercury: This salt gives quite good results in the majority of cases, but its action is uncertain. Sometimes a large extent of vein may become obliterated; at another time no result is obtained. Its injection does not cause "cramp". If injected into the tissues it gives rise to a very severe reaction and may cause extensive sloughing.

Even with intravenous injection a very violent reaction may occur, the affected vein becoming very swollen and red, with much pain for several days. In some cases the reaction is very wide-spread and is accompanied with edema of the foot.

There is at times a rather curious effect. The reaction at the original point of injection is followed by successive zones of inflammation extending one above the other along the course of the vein. This is rather alarming, but they have never been known to pass into the deeper veins. They remain limited to the affected vein.

Sometimes the reaction is delayed even a week or more, so it is not advisable at the beginning to give an injection oftener than once in 10-14 days.

It is most advisable to examine for signs of renal disease before using this drug.

I do not recommend this drug for routine use on account of the above mentioned reactions, but it is useful if Sod. Salicylate and Quinine fail and when there is a history of syphilis.

Citrate of Soda: The intravenous injection of this is attended with only slight cramp. The reaction may be very painful and necessitate rest in bed. Citrate of Soda does not present any special advantages, but is useful when owing to idiosyncrasy etc., it is inadvisable to use Quinine or Sod. Salicyl.

Sodium Chloride: This acts very well on the whole, but is apt to cause a great deal of cramp. This effect can be lessened by adding novocaine to the solution. Perivenous injection is very painful, and may lead to extensive necrosis. As this substance is non-toxic, a great many varices can be treated at one sitting.

Lomholt<sup>36</sup> reports a case of death after injection of strong Sod. Chloride solution.

Meisen's Solution: Meisen claims that this gives very successful results. When he used 25 c.c. of it at one sitting, he found that embolus might result and he now states that 10 c.c. is his maximum dose, and with this he says no embolus follows. We have never used this mixture. It seems preferable to use a single substance only, as the reaction is then definitely known. Polypharmacy is best avoided in intravenous injections.

Glucose: Acts very well in certain cases, but in others its effects are uncertain. It is a useful substitute for other injections, just as Citrate of Soda is.

It has been combined with Sod. Chloride, but not always with happy results. Olson<sup>37</sup> reports a case of embolus with fatal result following the injection of this mixture. ~~important that the solutions of the substances~~

~~info~~ It is non-toxic, and thus is suitable for treating a large area at one consultation. ~~fine needle (No. 19)~~

~~and a 2 c.c. Record Syringe. These are sterilized~~

~~by boiling. It is important that the bevel of the~~

#### SUMMARY.

~~syringe should be short, as this allows the point to~~

~~remain in the vein without piercing the opposite wall.~~

The above are the chief substances used in modern treatment. My preference is for two of them, Sod. ~~corn.~~ This helps to prevent leaking of blood.

Sal. and Quinine. My ordinary practice is to use ~~The skin is disinfected with absolute alcohol.~~

Sod. Salicylate. first. Should, however, it fail,

as it sometimes does with the larger varices, Quinine

is substituted, and this will practically always cause

a successful result. If patients have extensive

varices, and a quick result is necessary, the Quinine

is used from the first. It is, however, necessary to

warn them that this treatment may compel them to rest

in bed for a few days.

Quinine is also used instead of Sod. Salicylate when the patient is unable to endure the cramps which follow the injection of the latter substances.



the above position. TECHNIQUE. must stand up. This position is not possible for some very nervous patients.

It is essential to have perfect asepsis, and it is very important that the solutions of the substances injected should be made up by a reliable firm.

In my practice I use a very fine needle (No.19) and a 2 c.c. Record Syringe. These are sterilised by boiling. It is important that the bevel of the syringe should be short, as this allows the point to remain in the vein without piercing the opposite wall. The point must be very sharp so that the vein is not torn. This helps to prevent leaking of blood.

The skin is disinfected with absolute alcohol. The piston is slightly withdrawn and if the

Position of Patient: Where possible sitting on a high couch with the legs hanging over the edge. The operator can then sit on a low stool. Cotton wool held in position round the ankle then by an elastic band is a convenient way to catch any blood that trickles down the limb when the veins of the leg are operated on. If the veins are not sufficiently prominent in to run the ulnar border of the left hand upward from the

the above position, the patient must stand up. This position is not possible for some very nervous patients. A tourniquet applied round the thigh when the patient is standing will make the veins sufficiently prominent for the patient either to sit or even to lie down. It is only when the veins are very large that it is possible to treat them satisfactorily when lying down without previously applying the tourniquet.

The injection: One begins with the lower part of the vein first. The needle attached to the syringe filled with the chosen solution is pushed into the vein through the sterilised skin in an upward direction. The piston is slightly withdrawn and if the point of the needle is within the vein, blood will flow into the syringe. As small a quantity of blood as possible must be allowed to enter the syringe in order to avoid diluting the solution. The solution is then injected into the vein.

The object is to act on the intima of the vein. One gets the best results when the injected vein is most empty of blood and a satisfactory way in practice is to run the ulnar border of the left hand upward from the

site of puncture with slight pressure along two or three inches of the vein. It is kept there during the injection. When the desired amount of the solution has entered the vein, the needle is kept in position for about half a minute and then withdrawn, the puncture being immediately pressed on by sterilised cotton wool, held in the fingers of the left hand, and the limb elevated. The pressure not only helps to lessen oozing, but also prevents the dilution of the injected liquid by the flow of blood from the distal part of the vein. The leg is kept elevated for 2 or 3 minutes.

Sicard<sup>38</sup> recommends that the elevation of the limb should be a passive one. Should the patient raise the limb by muscular contraction there is the risk of drawing some of the injected fluid into the deep veins and setting up an inflammation in them. This opinion is based on the radiographic study of Lipiodol injected into the veins. He injected 1 c.c. Lipiodol into a dilated vein at the upper part of the leg, the patient being in the horizontal position. He noted that the Lipiodol tends to pass towards the foot, and as long as the patient does not move, it

varices which cannot be treated directly. The needle is passed into the vein with its point directed downwards in the direction of the foot and 5-10 c.c. of a



remains in the superficial plexus of veins, but if he move his leg, either by making flexion or extension movements, or by walking a short distance, much of the Lipiodol is found in the deep veins.

Of course my experience is nothing like that of Sicard's but in hospital practice it is not always possible to prevent patients from moving their limbs after an injection, and so far I have not seen any bad effects from their doing so.

If there is oozing at the end of that time when the leg is lowered, sterilised wool kept in position by an elastic band stops it and allows the operator to proceed with further punctures.

Some operators use a different proceeding. After the needle is in the vein, they raise the leg and then inject. This method is very good but requires care, lest the needle should pass out of the vein during the movement of the limb.

The first method is the one I prefer and it has answered very successfully.

Filderman<sup>39</sup> describes a method which he says is very useful when there are in addition very fine varices which cannot be treated directly. The needle is passed into the vein with its point directed downwards in the direction of the foot and 5-10 c.c. of a



20-30% Sod. Sal. solution are injected. This method is painful and requires the use of novocaine. We have never attempted it.

The method of Bardy<sup>40</sup> (ligature of the saphenous vein and injection of large quantities of Pregl's iodine solution) does not come within the scope of this paper. He is satisfied with his results.

#### Results of Treatment.

##### Clinical.

The patients very early in the treatment experience a sense of relief in their legs. The feeling of weight and the pain disappears. It is curious to note how this relief is noticed after only a few of the veins have been successfully treated. The appearance of the leg is much improved, and any oedema is greatly lessened or disappears. Varicose ulcers and skin eruptions are also greatly benefited. Indeed this treatment is the foundation of a successful result in these conditions. It helps the action of other remedies.

As regards the question of embolus resulting from the treatment, I have never yet seen a case and neither, as far as

I am aware has Sicard, Paraf or Genevrier. The experience of these three is enormous, and they have not reported a case. An injection which is not properly performed especially as regards ~~to~~ asepticity, may lead to the formation of a septic thrombus. This is not the fault of the treatment, but of the operator.

Another case in which embolus may occur is when a mixture of substances is injected into the vein, e.g., Cal<sup>o</sup>rose and Sod. Chloride, or Sod. Sal. and Sod. Chloride as has been previously mentioned. It is in my opinion much better to inject only one drug. One has then to deal with a definite reaction.

I do not think that the statement so frequently made that any embolus would tend to pass peripherally on account of the reversed flow of the blood in varicose veins is tenable.

So long as the patient is erect it may be so but there are positions in the patient's daily life when the normal direction of the blood current is resumed which would at once favour the passage of an embolus into the general circulation.

The claim that embolus does not occur must rest on the fact that the thrombus is so firmly adherent to

the vessel wall that it cannot be detached. The injection of the substance into the perivenous tissues or the passage of blood mixed with the injected substance into the tissues outside the vein, may cause very violent reactions attended with great pain and crippling. The remedies for these are obvious. A sharp needle, strictly intravenous injection, not too much haste in withdrawing the needle and firm pressure while the needle is being withdrawn.

or three days previously the elastic fibres are ruptured.

Microscopical. suggests tentatively that the painful cramps which follow intravenous injection may be due to their sudden rupture. This is hardly likely as the cramps occur aseptically. The venous wall becomes markedly swollen, all the coats participating, and in some cases the inflammation extends beyond the adventitia. This can be noted clinically in cases where the overlying skin becomes red.

The endothelium of the intima becomes swollen and in places desquamates. Its cells can be seen detached in the lumen of the vein. Over the area of damaged endothelium a clot is formed which is very firmly adherent. This clot is soon invaded by young vessels and



connective tissue cells. The acute congestion of the venous wall passes off and as a result of the proliferation of the connective tissue cells in the various coats of the vein, ultimately the vein is transformed into an impermeable fibrous cord<sup>in</sup> which all traces of the original structures (e.g. muscular tissue, elastic lamina, etc.) have practically disappeared.

A minor point may be mentioned. It has been found that in sections of veins which have been injected two or three days previously the elastic fibres are ruptured and Bazeles<sup>41</sup> suggests tentatively that the painful cramps which follow intravenous injection may be due to their sudden rupture. This is hardly likely as the cramps occur especially after treatment with Sod. Salicylate and are not noticeable as a rule with Quinine or Biniodide of Mercury. As mentioned above, I think they are reflex due to the special irritating action of the Sod. Salicylate.

Sicard in his numerous works refers to the changes in the veins as a "veinite", and in his earlier writing he uses the term "endoveinite" which seems to imply an inflammation limited to the intima of the vein.

I do not think that it is necessary to introduce a new term for the inflammation caused by these injections. The term phlebitis is the pathological name consecrated by custom and the facts that it is caused in this case by a chemical substance and that it is aseptic are surely not enough to justify a new pathological name. As regards the term endoveinitis, Sicard, as mentioned above, is more inclined to replace it by 'veinite' in his latest work<sup>42</sup> especially since the experiments of Jentzer of Geneva<sup>43</sup>, who injected into veins of rabbits and of man, solutions of Sodium Salicylate mixed well with collargol. The veins were excised 2 days, 4 days, 8 days, and 12 days after the injections. The collargol was found to have penetrated all the walls of the vein and had reached even the perivenous tissues. A reasonable inference was that the Sod. Salicylate must have done so also.

Apart from this the various microscopical examinations made lately have shown that all the venous walls take part in the process. As mentioned above, after an injection, there is great swelling of the venous walls and it is possible that in the smaller veins this swelling

is sufficient to completely obliterate the lumen without any clot being formed.

Among the various writers who have done experimental work on this part of the subject and who have also had opportunities of examining the vein in man may be mentioned Regard<sup>44</sup>, Delater and Hugel<sup>45</sup>, Meisen<sup>46</sup>, Bardy<sup>47</sup>, Montpellier Lacroix and Boulin<sup>48</sup>, Sicard<sup>49</sup>, Humbert<sup>50</sup>. The work of Jentzer had just been referred to.

In cases of pregnancy the same rule applies, even in those cases where the veins are enormously distended and seem as if some of them would burst, the case is best treated by rest in bed and bandaging. When the patient cannot lie in bed as much as is desirable, the application of a zinc gelatine dressing or bandage impregnated with zinc gelatine is all that is necessary to be done in the majority of these cases.

Should however rupture of a vein seem inevitable, it can be obliterated by one of the above mentioned substances, and a severe hæmorrhage avoided. Quinine of course must not be used for this purpose as it may cause abortion.

The same methods apply to cases of heart disease where



compensation has Contra-indications. the heart condition first, and deal with the veins afterwards if necessary.

Judging whether or not the attempt to cure the veins should be made is largely a matter of medical knowledge, plus common sense.

If the cause of the enlarged vein is some obstruction from a pelvic or abdominal tumour, the obvious remedy is to remove the tumour first, allow a reasonable time to elapse and then treat any remaining enlarged veins. In cases of pregnancy the same rule applies, even in those cases where the veins are enormously distended and seem as if some of them would burst, the case is best treated by rest in bed and bandaging. When the patient cannot lie in bed as much as is desirable, the application of a zinc gelatine dressing or bandage impregnated with zinc gelatine is all that is necessary to be done in the majority of these cases.

Should however rupture of a vein seem inevitable, it can be obliterated by one of the above mentioned

substances, and a severe haemorrhage avoided. Quinine of course must not be used for this purpose as it may cause abortion.

The same methods apply to cases of heart disease where

compensation has broken down. Treat the heart condition first, and deal with the veins afterwards if necessary.

I do not consider that high blood pressure caused by renal disease, arterio-sclerosis etc., is a necessary contra-indication. The case must be looked at as a whole, and if efforts to relieve the blood pressure are unsuccessful, and the veins are adding to the patient's distress, I should certainly obliterate them.

There is one condition where I consider that this should not be done and that is where there is definite indication of phlebitis of the deep veins of the leg. An attempt to do so is, in my opinion, wrong as it has been found by experience that it is apt to light up the old inflammation. Besides the varicose veins in this case are to be regarded as a compensatory enlargement, and to obliterate them would only increase the patient's distress. The best treatment is to support them by properly applied bandages.

In this connection, although somewhat apart from the subject of the paper, may be mentioned the condition termed by Vaquez, La Septicémie veineuse subaiguë<sup>51</sup> and studied also by Legrand.<sup>52</sup> This condition, according to Sicard, is frequently cured by intravenous injections of Sod. Salicylate,

but the strength should be weak, only 5-10%.

Patients with varicose veins are often subject to localised attacks of Phlebitis in them and the question arises; Is it safe to use the injection treatment? Certainly it ought not to be used until the attack of Phlebitis has completely disappeared. When this has done so the veins can be cautiously treated. The solution employed should be weak, e.g. 10-15% Sod. Salicylate and the amount injected should not be more than 2 c.c. The treatment should not be given often-er than once a week at most.

The reason for this care is that the veins under these circumstances have been found by experience to react much more than usual to irritants, so that the stronger solutions usually employed cause exceedingly severe sequelae.

Injection of course will not be made into the veins near a septic ulcer of the leg or through skin which is inflamed.

Another condition which is best left alone is when there are numerous small dilated venules. These are disfiguring of course, and the leg often feels spongy and



swollen. There have been attempts made to cure them, but personally I refuse to treat them unless there are large dilated veins which seem to be the cause of the dilatation of the venules.

I also avoid treatment in alcoholics and in cases of diabetes.

#### Summary.

There is one absolute contra-indication, i.e., previous phlebitis of the deep veins. In all other cases the operator must combine judgment and knowledge of general medicine, and if there are other methods of curing or relieving the varicose condition, he ought not to allow his zeal for the injection method of treatment to outrun his discretion.

The advantages of this method of treatment.

General Summary.

1. It is safe. So far I know of no case of embolus in cases treated on the lines I have indicated.
2. It is ambulatory: The patient can remain at work. It is only in a small percentage of cases that rest in bed is necessary and even then two or three days are sufficient. Of course I exclude here those patients whose mentality urges them to go to bed when they suffer the slightest pain or inconvenience.
3. It is curative: if the patient will persevere one can guarantee a cure in all those cases where proper selection and judgment have indicated the necessity for treatment.

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3. Quinine to be used when time is an object, when the veins are very large, when Salicylate has failed, or causes too much cramp.
4. If either Salicylate or Quinine is contra-indicated, e.g. from idiosyncrasy, etc., any of the other solutions may be used.
5. The cases in which either Salicylate or Quinine fail are exceedingly few.
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